REMARKS

In response to the office action dated January 9, 2008, Applicants have amended claims 1, 5-7, and 10 to more particularly point out and distinctly claim the subject matter which they regard as their invention. Support for claim 10 can be found at, e.g., page 10, lines 9-13 of the specification. Claims 1-7 and 10 are presented for examination.

Claims 1-7 and 10 are rejected under 35 U.S.C. §112, 1st paragraph as failing to comply with the written description requirement.

First, the Examiner asserts that "[t]he working examples are all drawn to where X is -O- and R1 is substituted phenyl ring. … The working examples are not representative of the entirely claimed genus since they are closely related to each other and do not show the full breadth of the genus claim." *See* the office action, page 2, lines 22-23 and page 3, lines 10-12. Applicants would like to point out that the present application is not the first example of using pharmaceutically active piperidine compounds for treating a chemokine mediated disease. For example, Applicants have described in an earlier published PCT application, i.e., WO 01/77101, similar piperidine compounds that can be used to treat a chemokine mediated disease. *See*, e.g., the Abstract of WO 01/77101. In these compounds, the group corresponding to X can be CH_2, NH, C(O), and $S(O)_2$ (*see*, e.g., compounds 1-5 in Table 5 on page 55 of WO 01/77101) and the group corresponding to R_1 can be either unsubstituted aryl or substituted and unsubstituted heterocyclyl (*see*, e.g., compounds 280, 282, 287, 292, 293, and 308 in Table 4 from pages 53-55 of WO 01/77101). Further, the present application describes in general on pages 7-10 how to prepare piperidine compounds in which X and R^1 are the groups recited in claim 1 (including those in which X is not -O- and R^1 is not substituted phenyl) and on pages 18-21 how to test these compounds for their therapeutic efficacy. Thus, in view of the present application and the knowledge in the art, a skilled artisan would readily recognize that Applicants are either in actual possession or in conceptual possession of the piperidine compounds of the entire scope of claims 1-7 and 10.

Second, the Examiner contends that "there is no evidence within the specification that shows a correlation between structure and function with any compound where R1 is not a substituted phenyl ring and where X is not -O-." *See* the office action, page 3, lines 12-14. Applicants would like to point out that a key feature of the claimed compounds is the specific

substituents attached to the nitrogen atom on the right piperidine group, i.e., the $CH(R^2)CO_2R^{24}$ group. The present application already provides 25 examples of piperidine compounds with different $CH(R^2)CO_2R^{24}$ groups, as well as their test results obtained from four biological assays. Once it has been shown that piperidine compounds with different $CH(R^2)CO_2R^{24}$ groups all exhibited therapeutic efficacy, one skilled in the art could reasonably extrapolate the compounds in which R^1 is a substituted phenyl ring and X is -O- to compounds in which R^1 is a common substituent (such as those assigned to R^1 recited in claim 1) other than a substituted phenyl ring and X is a common linking group (such as those assigned to R^1 recited in claim 1) other than -O-.

Third, the Examiner asserts that "the specification does not teach any interaction with chemokine [receptors] by the instantly claimed compounds. Instead, examples are provided to show binding with the histamine H1 receptor. How can one show possession of a method to treat chemokine diseases by showing how compounds interact with the histamine H1 receptor?" *See* the office action, page 3, lines 14-18. Applicants respectfully disagree. The present application describes in Example 25 an assay for testing the efficacy of a claimed compound in binding with eosinophils in the presence of eotaxin. It is well known in the art that eotaxin is an agonist of a chemokine receptor. *See*, e.g., the abstract and page 151, right column of Conroy et al., *Respir. Res*. 2001, 2:150-156, a copy of which is attached hereto as "Exhibit A." As shown in Example 25, the claimed compounds were found to be antagonists of eotaxin mediated human eosinophil chemotaxis. In other words, the results showed that the claimed compounds were able to bind chemokine receptors and therefore inhibit binding of eotaxin to chemokine receptors on eosinophils. Thus, the specification clearly teaches interaction between the claimed compounds and chemokine receptors.

Finally, the Examiner contends that "the claims are drawn to solvates, but the specification does not show how to make any solvates. One of skill in the art would not deem that one is in possession of a solvate unless the solvate has actually been made." See the office action, page 3, lines 18-20. Applicants do not agree with the Examiner's contention. However, to expedite prosecution of this application, Applicants have removed the term "solvate," all occurrences, from claims 1, 7, and 10.

For at least the reasons set forth above, Applicants submit that claims 1-7 and 10 are adequately described by the present specification. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

Claim 10 is rejected under 35 U.S.C. §112, 2nd paragraph as being indefinite. Specifically, the Examiner asserts that "[t]he claim is drawn to a method of treating chemokine mediated diseases, but does not detail which exact diseases are intended to be treated or which chemokine the compound will interact with." *See* the office action, page 4, lines 1-6. To expedite prosecution of this application, Applicants have limited claim 10 to specific diseases, i.e., autoimmune, inflammatory, proliferative, or hyperproliferative disease, rejection of transplanted organs or tissues, or Acquired Immunodeficiency Syndrome. Applicants submit that claim 10, as amended, is not indefinite and request reconsideration and withdrawal of this rejection.

Applicants submit that the pending claims are now in condition for allowance, an action of which is requested.

The fee in the amount of $120 for the Petition for One-Month Extension of Time is being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization. Please apply any other charges to deposit account 06-1050, referencing Attorney's Docket No. 06275-417US1.

Respectfully submitted,

Date: May 7, 2008

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